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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,371	03/07/2001	Raymond Kaempfer	A34084 PCT USA-A	9946

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

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19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/801,371	KAEMPFER ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *32-46 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 7-11* is/are rejected.

7)☒ Claim(s) *4-6,12-31 and 47-49* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Non-Final Rejection

Claims 1-31 and 47-49 are pending examination.

Election/Restrictions

Applicants elected group I (claim 1-31 and 47-49) without traverse in paper no. 18.

Claims 32-46 and 50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 18.

Cancellation of claims 32-46 and 50 in paper no. 18 is acknowledged.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d) for Israel 126112 and 126757, which papers have been placed of record in the file.

Information Disclosure Statement

The patent documents in information disclosure statement filed 6/12/01 will not be initialed and considered by the examiner because they are duplicates of patent documents in IDS filed on 9/4/01.

Examiner cannot locate the IDS filed on 5/14/01, for the examiner's convenience please submit the IDS again with the response to this office action.

The information disclosure statement filed on 9/4/01 does not fully comply with the requirements of 37 CFR 1.98 because: applicant does not properly cite the journal article(s) listed on the 1449. The title of each journal article is missing.

The examiner has considered the references, but in order to have them initialed and dated on the 1449, a new 1449 properly citing the journal articles must be filed with the response to this office action. Failure to comply with this notice will result in the above mentioned information disclosure statement being placed in the application file with the non-complying information not being considered. See 37 CFR 1.97(i).

NOTE: In addition, several journal articles in information disclosure statement filed 6/12/01 will not be initialed and considered by the examiner because they are duplicates of journal articles in IDS filed on 6/12/00 that were initialed and considered by the examiner.

The international search report and preliminary examination report has been considered.

Drawings

The drawings are acceptable.

Claim Objections

Claims 4-6, 12-31 and 47-49 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend on another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 4-6, 12-31 and 47-49 have not been further treated on the merits.

Claims 1 and 7 are objected to because of the following informalities: the term "intron/s". Appropriate correction is required.

Claim 11 is objected to under MPEP 2173.05(h), as using improper Markush group language. The claim recites, "group consisting of enzymes, hormones, growth factors, cytokines, structural proteins and industrially or agriculturally applicable proteins, or is itself a therapeutic product, and agricultural product, or an industrially applicable product." The terminology

(using several and/or) in the claim is unacceptable Markush group language. The dependent claim should be recited in the conventional or alternative manner.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because of the term "said" on line 3, intron/s on line 2, and the abstract is more than 150 words. Correction is required. See MPEP § 608.01(b).

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3 and 7-11, as best understood, are readable on a genus of a cis-acting nucleotide sequence, wherein the genus of sequences is capable of rendering the removal of intron(s) from a pre-cursor transcript encoded by a gene, is not claimed in a specific biochemical or molecule structure that could be envisioned by one skilled in the art at the time the invention was made.

The specification described one cis-acting nucleic sequence, which is set forth in SEQ ID NO: 1 and forms a stable, 5'proximal 48-nt stem-loop containing 17 base pairs set forth in SEQ ID NO: 2 (Table 1). Furthermore, the as-filed specification contemplates biological functional fragments, derivatives, mutants and homologues of the nucleotide sequence substantially as denoted by SEQ ID NO: 1. The disclosure provides sufficient description for SEQ ID NO: 1. However, the as-filed specification does not provide sufficient description of a genus of cis-acting nucleotide sequence. It is not apparent that on the basis of the applicants' disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the claimed invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of cis-acting nucleotide sequence that must exhibit the disclosed biological functions as contemplated by the specification.

More specifically, the as-filed specification does not provide an adequate written description of a representative number of species of cis-acting nucleotide sequence. It is apparent from the state of the prior art exemplified by Ngo *et al.* (The Protein Folding Problem

and Tertiary Structure Prediction, Birkhauser Boston, 1994, pp. 491-494) and Chiu *et al.* (*Folding and Design*, Vol. 3, 1998, pp. 223-228) that the description of the primary sequence of amino acid residues in which the positions of the amino acid residues are particularly arranged is essential for the biological function of the protein encoded by the sequence. This essential element that is required for an adequate description of a representative number of species as embraced by the claimed genus of cis-acting nucleotide sequence is neither described sufficiently in the specification nor conventional in the prior art. A mere statement asserting that any sequence with biological functional fragments, derivatives, mutants and homologues of the nucleotide sequence substantially as denoted by SEQ ID NO: 1, without providing the essential and specific arrangement of the amino acid residues positioned in the sequence does not lend evidentiary support for a skilled artisan to have recognized that applicant was in possession of the genus of cis-acting nucleotide sequence as claimed, particularly since the essential element of the coding sequence of a generic cis-acting nucleotide sequence is lacking from the as-filed specification and since the skill and knowledge in the art is not adequate or conventional to determine the primary sequence of the representative number of species of cis-acting nucleotide sequence or nucleic acids on the basis of the only disclosure of SEQ ID NO: 1.

It is not sufficient to support the present claimed invention directed to the genus of cis-acting nucleotide sequence. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of cis-acting nucleotide sequence that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in

compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of cis-acting nucleotide sequence that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 1-3 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) A cis-acting nucleotide sequence comprising the 3' untranslated region of the human tumor necrosis factor alpha gene set forth in SEQ ID NO: 1 or consisting of SEQ ID NO: 2, which removes intron(s) from a pre-cursor transcript encoded by a gene, wherein said gene comprises at least one of said cis-acting nucleotide sequence and is dependent upon activation of a trans-acting factor, wherein said trans-acting factor is the RNA-activated protein kinase (PKR), which capable of phosphorylating the alpha subunit of eukaryotic initiation factor 2 (eIF2), 2) A DNA construct comprising: a gene, which contains at least one intron; cis-acting nucleotide sequence comprising the 3' untranslated region of the

human tumor necrosis factor alpha gene set forth in SEQ ID NO: 1 or consisting of SEQ ID NO: 2, which removes intron(s) from a pre-cursor transcript encoded by a gene, wherein said gene comprises at least one of said cis-acting nucleotide sequence and is dependent upon activation of a trans-acting factor, wherein said trans-acting factor is the RNA-activated protein kinase (PKR), which capable of phosphorylating the alpha subunit of eukaryotic initiation factor 2 (eIF2); and optionally comprising additional control, promoting and/or regulatory elements, and does not reasonably provide enablement for the full breadth of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Specifically, since the claimed invention is not supported by a sufficient description (for possessing a genus of cis-acting nucleotide sequence) as recited in the claims, particularly in view of the reasons set forth above, one skilled in the art would not have known how to make and use the claimed invention so that it would operate as intended, e.g. capable of rendering the removal of intron(s) from a pre-cursor transcript encoded by a gene.

Even if the applicants are able to overcome the written description rejection set forth above, there are concerns under 112 enablement for the claimed genus of cis-acting nucleotide sequences.

The claimed invention encompasses modulating gene expression using a cis-acting nucleotide sequence, which renders the removal of introns from pre-cursor transcript encoded by

a gene of interest. The field of the invention lies in nucleotide sequences that could be used as cis-acting nucleotide sequence, e.g. TNF-alpha 3'UTR.

At the time the application was filed, predicting any protein tertiary structure based on a protein structure was considered to be unpredictable due to significant problems in several areas. The state of the art in 1998, exemplified by Chiu et al., *Folding and Design*, Vol. 3, pg. 223-228, May 1998, displays major consideration for predicting a protein tertiary structure involve issues that include:

> Predicting the three-dimensional conformation of a correctly folded protein can be divided into two distinct steps: the construction of a fitness function to evaluate the various conformations: and the search through various possible conformations for the "best" prediction most likely to represent the native state. Neither part of this problem has proven particularly tractable. The development of a general method for the prediction of protein tertiary structure based on the protein sequence remains, unfortunately, one of the great-unsolved problems of computational biophysics (pg. 223).

Furthermore, Ngo et al. display that the relationship between the sequence of a peptide and its tertiary structure of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable.

The as-filed specification teaches that the cis-acting element in the human TNG-alpha 3'UTR renders splicing of TNF-alpha mRNA sensitive to inhibition by 2-Aminopurine (AP), and contemplates that this is a unique and novel tool for bringing expression of a desired gene under the control of this mechanism. The state of the art exemplified by Jarrous teaches a method of regulating gene expression at the mRNA level transforming a host cell with a vector comprising the TNF-alpha gene, including the 3' un-translated region, wherein the activity of the RNA activated eIF2alphakinase in the host cells is modulated by the use of 2-AP (IDS, page 2820, column 1, lines 5-24). Jarrous further teaches that, "Most likely, regulation by 2-AP is

mediated through a particular sequence within the TNF-alpha primary transcript to produce general inhibition of the splicing of this transcript (page 2821) and that "..deletion of a particular sequence from the TNF-alpha gene renders splicing of the encoded pre-cursor transcripts resistant to inhibition by 2-AP, while introduction of said sequence into the TNF-beta shifts inhibitory effect of 2-AP on the TNF-beta gene expression from transcription to splicing (page 2821). The as-filed specification locates the sequence through genetic techniques that Jarrous speculates about in the TNF gene (see pages 26-41).

In view of the In re Wands Factors, the claimed invention is only enabled for cis-acting nucleotide sequence set forth in SEQ ID NO: 1 and SEQ ID NO: 2 and is not enabled for the full breath of the claimed invention. The claimed invention is broader (biologically functional fragments, derivatives, mutants and homologues of the nucleotide sequence set forth in SEQ ID NO: 1, sequences whose complementary sequence hybridizes under conditions which allow for such hybridization to occur, or **derived** from the 3' un-translated region of human tumor necrosis factor alpha gene) than the enabling disclosure because there is no guidance as to which amino acids of the nucleotide sequence set forth in SEQ ID NO: 1 or 2 may be changed while cis-acting activity is retained. The state of the art (IDS, Jarrous et al., Molecular and Cellular Biology, Vol. 16, 1996, 2814-2822) teaches that two genes (TNF-beta and IL-1beta) have a similar sequence to TNF alpha and do not show that 2-AP blocks their mRNA unlike TNF-alpha (page 2814). In view of the art of record (e.g. Chui and Ngo), it would require undue experimentation for one skilled in the art to arrive at other sequences that are cis-acting nucleotide sequences. In Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences with a particular function that needs to be

determined subsequence to the construction of the sequences may not find sufficient support under 35 U.S.C. 112, first paragraph, if only a few of the sequences that meet the functional limitation of the claim are disclosed and if undue experimentation would be required for one skilled in the art for the determination of other sequences that are embraced by the claims. If it would require undue experimentation to identify other sequences that have cis-acting activity, it certainly would require undue experimentation to make the genus of cis-acting nucleotide sequences. This is the case here. Therefore, it would be reasonable to conclude that it would require undue experimentation to make the entire scope of the claimed invention.

In addition, with respect to claim 8 encompassing sequences whose complementary sequence hybridizes under conditions, which allow for such hybridization to occur, with the nucleotide sequence of a) or b). The claimed invention fails to provide sufficient guidance for one skilled in the art to practice the full breadth of the claim because one skilled in the art would be able to use SEQ ID NO: 1 or 2 to probe for sequences that completely complement SEQ ID NO: 1 or 2. However, a nucleotide sequence whose complementary nucleotide sequence hybridizes with biologically functional fragments, derivatives, mutants and homologues of the nucleotide sequence substantially as denoted by SEQ ID NO: 1 comprises an enormous number of nucleotide sequences that would not meet the structural and/or functional limitation of claims. Furthermore, the nucleotide sequences encompass any nucleic acid sequence (e.g. 10 nucleotides to 1,000 nucleotides) that would not have cis-acting activity and the as-filed specification does not provide sufficient guidance for one skilled in the art to reasonably determine which nucleotide sequences have cis-acting nucleotide activity. Therefore, it would take one skilled in the art an undue amount of experimentation to make and/or use claimed sequences whose

complementary sequence hybridizes under conditions, which allow for such hybridization to occur, with the nucleotide sequence of a) or b).

Furthermore, with respect to using a trans-acting factor in claims 1-3 and 7-11, wherein said trans-acting factor is an RNA-activated protein kinase which is capable of phosphorylating the alpha-subunit of eIF2, the as-filed specification only provides sufficient guidance for one skilled in the art to use PKR (pages 21-22) and not for the full breadth of the claimed RNA-activated kinases which is capable of phosphorylating the alpha-subunit of eIF2. The state of the art teaches that two types of kinases (PKR and heme) that are capable of phosphorylating the alpha-subunit of eIF2 (IDS, Jarrous, page 2814, 1996). However, the as-filed specification does not provide sufficient guidance for one skilled in the art to reasonably determine of heme kinases can be used in the claimed product. Jarrous teaches that, "Both activations of PKR and its inhibition require highly ordered RNA structures rather than specific sequences (IDS, Osman et al., Genes & Development, Vol. 13: 32980-3293). The art of the record and the as-filed specification fail to provide sufficient guidance for one skilled in the art to reasonably determine whether heme kinases share a similar high ordered RNA structure. Therefore, it is not apparent that heme kinases could be used as a trans-acting factor for the claimed cis-acting nucleotide sequence. Thus, the claimed invention is only enabled for using PKR as the trans-acting factor.

In conclusion, in view of the In Re Wands Factors, the claimed invention is only enabled for 1-2 listed above and not for the full scope of the claimed embodiment. It is not apparent how one skilled in the art can make and/or use the genus of cis-acting nucleotide sequences, given that predicting the sequence of any and/or all protein tertiary structures based on a protein sequence remains an unsolved problem. Therefore, one skilled in the art would have to engage

in a large quantity of experimentation in order to practice the claimed invention based on the applicant's disclosure and the unpredictability of predicting a polypeptide sequence based on the primary sequence.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 2, 8-9, and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The statement in claim 2, "**A** cis-acting nucleotide sequence" is indefinite because it does not point out which sequence **a** cis-acting nucleotide sequence is referring to in the claim. Claim 2 is not a multi-dependent claim. The dependent claim should state "**The** cis-acting nucleotide sequence".

The statement in claims 8-9 and 11, "**A** DNA construct according to claim 7" is indefinite because it does not point out which construct **a DNA construct** is referring to in the claim. Claims 8-9 and 11 are not multi-dependent claims. The dependent claim should state "**The** DNA construct according to claim 7".

The term "such" in claim 8 is a relative term, which renders the claim indefinite. The term "such" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The disclosure does not define the metes and bounds of the term. The intended scope of the claim is unclear.

The phrase "substantially as denoted by SEQ ID NO: 1" in claims 8 and 9 is a relative phrase, which renders the claim indefinite. The phrase "substantially as denoted by SEQ ID NO: 1" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The claims do not particularly point out and distinctly claim what are the metes and bound of the phrase "substantially as denoted by SEQ ID NO: 1". More specifically, the disclosure does not define the metes and bounds of the phrase because it is not apparent if 1%, 10%, 50%, 99%, etc. constitutes the definition for the term "substantially".

The term "itself" in claim 11 is a relative term, which renders the claim indefinite. The term "itself" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The disclosure does not define the metes and bounds of the term. It is not apparent whether "itself" is referring to the protein or said gene in the claim. Clarification is requested.

Claim 11 recites the limitation "said gene encodes a protein" in claim 11. There is insufficient antecedent basis for this limitation in the claim. Claim 7 which claim 11 depends from does not recite said limitation. Claim 7 recites, "a gene which contains at least one intron".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Pennica et al. (IDS, Nature, Vol. 312, 1984, pp. 724-729). Pennica discloses the nucleotide sequence of the human TNF-alpha gene including SEQ ID NO: 1 and 2, which reads on a cis-acting nucleotide sequence of the present application (see page 725, Figure 1).

Claims 1-3 and 7-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Jarrous et al. (IDS, Mol. Cell. Biol., Vol. 16, 1996, pp. 2184-2822). Jarrous discloses a vector comprising the TNF-alpha gene including the 3' untranslated region, which reads on a cis-acting nucleotide sequence of the present application (see page 2820). Jarrous further teaches that the trans-acting factor for the sequence is PKR (page 2814).

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kay Pinkney whose telephone number is (703) 305-3553.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, primary examiner, Dave Nguyen can be reached at (703) 305-2024.

If attempts to reach the primary examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635
10/31/02

DAVE T. NGUYEN
PRIMARY EXAMINER